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Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/066,474 | NICOLETTE, CHARLES A. | |
| | Examiner | Art Unit | |
| | Stephen L. Rawlings, Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *November 21, 2003 and April 20, 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *2-6,11-13,15,16,19-21 and 27-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-10,14,17,18 and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2[illegible]3.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *IDS 20030311*.

## DETAILED ACTION

1. The election without traverse and the supplemental election with traverse, which were filed November 21, 2003 and April 20, 2004, respectively, are acknowledged and have been entered. As clarified during the interview of April 29, 2004, Applicant has elected Group IV, claims 1, 7-10, 14, 17, 18, and 22-26, insofar as the claims are drawn to a method for aiding in the diagnosis of a neoplastic condition, or a susceptibility thereto, wherein said method comprises determining the amount of expression of a MART-1 protein by detecting the amount of said protein using an agent that specifically recognizes and binds said protein, wherein said agent is an antibody or antigen-binding fragment thereof, which has been prepared using an animal immunized with the peptide of SEQ ID NO: 5, and a diagnostic kit comprising antibody or antigen-binding fragment.

2. Claims 1-29 are pending in the application. Claims 2-6, 11-13, 15, 16, 19-21, and 27-29 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the paper filed April 20, 2004.

3. Claims 1, 7-10, 14, 17, 18, and 22-26, insofar as the claims are drawn to the elected invention, are currently under prosecution.

### *Election/Restrictions*

4. In the paper filed April 20, 2004, Applicant has traversed the restriction and election requirement set forth in the Office action mailed October 21, 2003. Applicant has argued the restriction is improper because the inventions are closely related and can be searched and examined together without serious burden.

Applicant's arguments have been carefully considered but have not been found persuasive for the following reasons:

The inventions are related; and in fact, it has been acknowledged by the Office that claims 1, 3, 8, and 9-11 are linking claims. Nevertheless, the groups of inventions are distinct for the reasons set forth in the Office action mailed October 2, 2003. The search required for examination of any one of the groups of inventions is not coextensive with that that would be required to examine any other; and thus examination of each group of inventions requires a unique and different search. Consequently, searching more than one group of inventions would necessitate more than one search and would therefore constitute a serious burden. MPEP § 803 states restriction is proper, where the groups of inventions are unrelated or distinct and searching the entire application would constitute a serious burden. Moreover, the Office does not now have the facilities and resources that would be required to search more than one invention at this instance; however, as noted at page 4 of the Office action mailed October 21, 2003, the restriction requirement among the linked inventions is subject to the non-allowance of the linking claims and upon allowance of a linking claim, the restriction requirement as to the linked inventions shall be withdrawn and any claim depending from or otherwise including all the limitations of the allowable linking claim will be entitled to examination in the instant application.

Therefore, the restriction and election requirement is deemed proper and is made FINAL.

### *Information Disclosure Statement*

5. The information disclosures filed August 26, 2002, January 13, 2003, and March 11, 2003 have been considered. An initialed copy of each is attached hereto.

### *Oath/Declaration*

6. The declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The declaration is defective because this application is a continuation-in-part of US Application No. 09/922,405 and yet it does not acknowledge Applicant's duty to disclose intervening art.

### *Specification*

7. The disclosure is objected to because the disclosure refers to embedded hyperlinks and/or other forms of browser-executable code and to the Internet contents so identified. Reference to hyperlinks and/or other forms of browser-executable code and to the Internet contents so identified is impermissible and therefore requires deletion.

Examples of such impermissible disclosures appear, for example, at page 11 (paragraph [068]) and page 23 (paragraph [0108]).

The attempt to incorporate essential or non-essential subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP § 608.01(p), paragraph I regarding acceptable incorporation by reference.

### *Claim Objections*

8. Claims 17 and 18 are objected to because the claims are drawn in the alternative to the subject matter of non-elected inventions.

### *Claim Rejections - 35 USC § 112*

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 7-10, 14, 17, 18, and 22-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1, 7-10, 14, 17, and 18 are drawn to a method for aiding in the diagnosis of a neoplastic condition, or a susceptibility thereto, of an animal cell or tissue, wherein said method comprises determining the amount of expression of a MART-1 protein in a test sample isolated from said cell or tissue and diagnosing said neoplastic condition, or the susceptibility thereto, "based on" the amount of expression of the MART-1 protein, wherein the amount is at least 2-fold greater than the amount expressed in a normal or control sample, wherein the determination is made by probing the test sample with an agent that specifically recognizes and binds the protein. Claims 22-26 are drawn to a "diagnostic" kit comprising an agent that specifically recognizes and binds MART-1 protein.

The amount of guidance, direction, and exemplification set forth in the specification would not be sufficient to enable the skilled artisan to use the claimed invention to treat cancer without having the need to perform additional, undue experimentation. Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

To the extent that claims 1, 7-10, 14, 17, and 18 are drawn to a method comprising diagnosing a neoplastic condition, or the susceptibility thereto, "based on" the amount of expression of the MART-1 protein, while the skilled artisan could readily make the determination of the amount of MART-1 protein in a cell or tissue sample using an anti-MART-1 antibody, or antigen-binding fragment thereof, the specification provides an insufficient amount of guidance and direction to enable the skilled artisan to diagnose different neoplastic conditions on the basis of such a determination, since it appears that the specification fails to teach *how* the diagnosis should be based upon the result of the determination. Accordingly, the skilled artisan would have to perform an undue amount of additional experimentation to determine how to make a diagnosis

using the claimed invention. For example, given a particular type of neoplasm (e.g., breast cancer), because the specification fails to teach what amount of expression of MART-1 characterizes that neoplasm, the skilled artisan would have to first determine whether the amount of expression of MART-1 is even associated with that neoplasm, i.e., determine whether or not breast cancer, for example, characteristically expresses the normally melanocyte-specific MART-1. Similarly, with regard to claims 22-26, the amount of guidance, direction, and exemplification provided by Applicant's disclosure would not be sufficient to enable the skilled artisan to use the claimed invention diagnostically, since it appears the specification fails to teach how the kit can be used to diagnose any given disease or pathology, including a neoplastic condition. Again, given any particular disease or pathology, the skilled artisan would have to perform an undue amount of additional experimentation to determine how to make a diagnosis using the claimed invention.

The claims are broadly drawn to a method for diagnosing any type of neoplasm; however, there is no objective evidence presented by Applicant that MART-1 is associated with any given type of neoplasm (e.g., breast cancer; colon cancer). In fact, Wrightson et al. (*J. Surg. Res.* **98**: 47-51, 2001) have used lymph node tissue isolated from patients diagnosed with either breast or colon cancer as a negative control in an diagnostic analysis that measures MART-1 expression levels in lymph nodes isolated from patients diagnosed with melanoma. Wrightson et al. therefore provides factual evidence that suggests the claimed invention cannot be used to diagnose the presence of breast and colon cancer cells in lymph node biopsy tissue. Because the skilled artisan cannot predict which cells or tissues will express MART-1 upon neoplastic transformation, an undue amount of additional experimentation would have to be performed before the skilled artisan could use the claimed invention, because it would first be necessary to determine which types of neoplasia can be diagnosed on the basis of the result of a determination of the amount of expression of MART-1 in the cells or tissue.

More generally, Ward (*Developmental Oncology* **21**: 91-106, 1985) teaches, not all markers can be reliably used in primary diagnosis; moreover, Ward teaches that a

number of tumor-associated markers are, in fact, diagnostically unreliable (see abstract). Ward teaches some markers are more useful as guides in monitoring the efficacy of treatment modules for malignant disease (see abstract).

Tockman et al (*Cancer Research* **52**: 2711s-2718s, 1992) teach considerations necessary in bringing a cancer biomarker (intermediate endpoint marker) to successful clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to risk assessment, diagnosis, and/or prognosis of any type of cancer. Tockman et al teach that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence, and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and **if validated** (emphasis added) can be used for population screening (page 2713, column 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and link those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate endpoint marker (page 2714, column 1). Clearly, prior to the successful application of newly described markers, these must be validated against acknowledged disease end points; and, the marker predictive value must be confirmed in prospective population trials (page 2716, column 2).

Then, to the extent that claims 1, 7-10, 14, 17, and 18 are drawn to a method for aiding "diagnosing" a cell or tissue's susceptibility to neoplastic transformation, while the skilled artisan could readily make the determination of the amount of MART-1 protein in a cell or tissue sample using an anti-MART-1 antibody, or antigen-binding fragment thereof, the specification provides an insufficient amount of guidance and direction to enable the skilled artisan to determine whether a given cell or tissue is susceptible to

neoplastic transformation on the basis of such a determination, since it appears that the specification fails to teach *how* the determination should be based upon the result of the determination.

Only recently, and notably after the filing date of the instant application, has there been any report that the level of expression of MART-1 is an indication of the prognosis of a melanoma patient; see, e.g., Takeuchi et al. (*Cancer Res.* **63**: 441-448, 2003) and Berset et al. (*Int. J. Cancer* **95**: 73-77, 2001). However, there have been no reports, before or after the filing date of the instant application, that the level of expression of MART-1 is indicative of a cell or tissue's increased susceptibility to neoplastic transformation; and Applicant's disclosure of the claimed invention fails to provide any factual evidence that the level of expression of MART-1 can be used to determine whether or not a cell or tissue is more or less susceptible to neoplastic transformation. Therefore, the skilled artisan could not use the claimed invention to "diagnose" a susceptibility to a particular neoplastic condition without the need to perform an undue amount of additional experimentation to determine if the level of expression of MART-1 is a cell or tissue is predictive of the risk that the cell or tissue will become neoplastic.

Furthermore, with particular regard to claim 14, which is drawn to the method of claim 7 wherein the test sample is isolated from a melanocyte, because a melanocyte normally expresses an amount of MART-1 that is at least 2-fold greater than an amount expressed by a control sample (e.g., a normal non-melanocytic cell), a melanocyte expressing MART-1 cannot be said to be more or less susceptible to neoplastic transformation on the basis of the amount of expression of MART-1.

Insofar as the claims 1, 7-10, 14, 17, and 18 are drawn to a method comprising determining the amount of expression of a MART-1 protein by probing the sample with "an agent that specifically recognizes and binds" MART-1, while the skilled artisan could readily make an anti-MART-1 antibody, or antigen-binding fragment thereof, for use in practicing the claimed method, the specification provides an insufficient amount of guidance, direction, and exemplification to enable the skilled artisan to make other types of agents that specifically recognize and bind MART-1. Because the specification discloses at page 53 that the agent can be anything that binds MART-1, the agent could

be a ligand of MART-1, for example, but because the specification has not described a ligand of MART-1, the skilled artisan could not make the agent, which is a ligand of MART-1, without the need to perform an undue amount of additional experimentation to identify such a ligand and/or determine how such a ligand can be made. One cannot make what has not been described, and therefore amount of guidance, direction, and exemplification that is provided by Applicant's disclosure of the claimed invention is not reasonably commensurate in scope with the claims.

11. Claims 1, 7, 8, 14, and 22-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a written description rejection.

Claims 1, 7, 8, 14, and 22-26 are directed to an agent that specifically recognizes and binds MART-1. At page 53 (paragraph [0211]), the specification discloses that the agent can be any agent (such as a compound or cell) that binds to the protein. At page 53 (paragraph [0212]), for example, the specification discloses that such an agent can be a ribosome with or without a peptide component, an RNA molecule, a host cell comprising epitope, an immune effector cell, a peptide, an antibody, or a fragment of an antibody.

Accordingly, the claims are drawn to a genus of agents, which vary in markedly in both structure and function, and are merely described as commonly specifically recognizing and binding MART-1. Apart from an anti-MART-1 antibody, or an antigen-binding fragment thereof, Applicant's instant disclosure of the claimed invention does not adequately describe members of the genus of agents in sufficient detail to allow the skilled artisan to instantly envision, recognize, or distinguish at least a substantial number of the agents to which the claims are directed.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of

ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016.

In deciding *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the Court held that a generic statement that defines a genus of nucleic acids *by only their functional activity* does not provide an adequate written description of the genus. By analogy, a generic statement that defines a genus of agents by only their common ability to recognize and bind MART-1 does not serve to adequately describe the genus as whole. The Court indicated that while applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a precise definition of a representative number of members of the genus, such as by reciting the structure, formula, chemical name, or physical properties of those members, rather than by merely reciting a wish for, or even a plan for obtaining a genus of molecules having a particular functional property. The recitation of a functional property alone, which must be shared by the members of the genus, is merely descriptive of what the members of genus must be capable of doing, not of the substance and structure of the members.

*The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement* (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by

disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). The *Guidelines* state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

In addition, claim 24 is drawn to a kit comprising an agent that is immobilized on "chip". At page 51 (paragraph [0206]), the specification discloses that the agent can be immobilized on a solid support composed of nitrocellulose, latex, or plastic; however, it does not appear that the specification describes a solid support on which the agent can be immobilized, which is composed of a material designated "chip". Absent a description of a material designated "chip" on which the agent can be immobilized, the instant disclosure would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1, 7-10, 14, 17, and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 7-10, 14, 17, and 18 are indefinite because claim 1 recites, "the neoplastic condition" in line 1. There is a lack of antecedent basis to support the limitation; therefore, it cannot be determined to which neoplastic condition the claim is directed.

Claims 1, 7-10, 14, 17, and 18 are vague and indefinite because claim 1 recites, "based on". There is insufficient guidance in the specification to determine how, in practicing the claimed invention, the diagnosis is based on the amount of expression of the MART-1 protein; therefore, the skilled artisan would not be reasonably apprised of the metes and bounds of the subject matter that Applicant regards as the invention.

Claims 7 and 14 are indefinite because claim 7 recites, "said expression". There is a lack of antecedent basis in claim 1 to support the limitation. Amending claim 7 to recite, "said level of expression" can obviate this ground of rejection.

Claims 8-10, 17, and 18 are indefinite because claim 8 recites, "said detected". Even if "detected" is a misspelling of "detection", there is a lack of antecedent basis in claim 1 to support the limitation. The metes and bounds of the claimed invention cannot be determined.

Claim 9 is indefinite because the claim recites, "that specifically recognizes or binds". An immunoglobulin variable domain does not recognize or bind an antigen, which is recognized and bound by the immunoglobulin, e.g., an antibody, comprising the immunoglobulin variable domain. An antibody, which recognizes and binds a particular antigen, comprises two variable domains (a "light chain" variable domain and a "heavy chain" variable domain), which are either contained by a either single polypeptide chain or by two different polypeptide chains, that interact to form the antigen binding site. In addition, claim 9 is indefinite because the claim recites, "an antigen binding fragment thereof". Since an immunoglobulin variable domain does recognize or bind an antigen, an immunoglobulin variable domain does not comprise an antigen-binding fragment. Accordingly, the claim fails to meet the requirements set forth under

35 USC § 112, second paragraph by particularly pointing out and distinctly claiming the subject matter that Applicant regards as the invention.

Claim 17 is indefinite because the claim recites, "is prepared from an animal". While an animal can be used to prepare a monoclonal antibody, a monoclonal antibody is not prepared from an animal *per se*, but rather from a hybridoma or a recombinant cell. Accordingly, the claim fails to meet the requirements set forth under 35 USC § 112, second paragraph by particularly pointing out and distinctly claiming the subject matter that Applicant regards as the invention.

Claim 26 is indefinite because the claim recites, "wherein said detecting is" a member of a Markush group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin, and dye particles. While the step of detecting could involve detecting one of the members of the Markush group; however, as the claim is presently written, the metes and bounds of the subject matter that Applicant regards as the invention cannot be determined, since the claim is nonsensical (i.e., "detecting" cannot be, for example, biotin).

***Claim Rejections - 35 USC § 102***

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1, 7-10, 14, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Blessing et al. (*Histopathology* **32**: 139-146, 1998).

Claims 1, 7-10, and 14 are drawn to a method for aiding in the diagnosis of a neoplastic condition of an animal cell or tissue comprising determining the amount of expression of MART-1 protein in a test sample isolated from the cell or tissue and diagnosing the neoplastic condition based on the amount of expression of the MART-1

protein determined, wherein said determination is made by probing the test sample with an antibody that binds specifically to MART-1. Claim 22 is drawn to a kit comprising one agent that specifically recognized and binds MART-1, such as an antibody produced by immunizing an animal with a MART-1 antigen.

The Random House Dictionary (copyright © 1980, 1978 by Random House Inc.) defines the term "diagnosis" at page 242 as "the process of determining by examination and analysis the nature and circumstances of a diseased condition", or alternatively as "the conclusion reached from such a process". Accordingly, the claims are drawn to a process of determining by examination and analysis the nature and circumstances of a neoplastic condition comprising determining and comparing the expression of MART-1 in a test sample isolated from cells or tissue.

Blessing et al. teaches a method for aiding in the diagnosis of melanocytic lesions, particularly malignant melanoma, which comprises measuring the level of expression of MART-1 using an antibody that binds specifically to MART-1; see the entire document (e.g., the abstract). Blessing et al. teaches "Melan-A", an antibody that binds to the protein encoded by *MART-1* gene, stains only naevus cells (atypical melanocytes) and melanoma cells with no staining of the other components of normal skin (page 140, column 2); accordingly, Blessing et al. teaches the amount of MART-1 in the test sample isolated from the naevus and melanoma cells is at least 2-fold greater than the amount in a normal or control sample. Blessing et al. teaches the antibody is commercially available (page 140, column 1). Absent a showing of any difference, the commercially available, prepackaged container containing the antibody of Blessing et al. is deemed the same as the kit of claim 22.

### *Claim Rejections - 35 USC § 103*

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious

> at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 22-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blessing et al. (*Histopathology* **32**: 139-146, 1998) in view of US Patent No. 6,232,086 B1.

Claims 22-26 are interpreted to be drawn to a diagnostic kit comprising an monoclonal antibody that specifically binds MART-1, wherein said antibody is immobilized on a solid support, such as latex or plastic, and which kit further comprises a fluorescently-labeled secondary anti-immunoglobulin antibody for use as a detection reagent.

Blessing et al. teaches that which is set forth above. In addition, Blessing et al. teaches the immunoassay in which MART-1 is detected using the antibody that binds specifically to MART-1 involved "a standard indirect ABC technique" (page 140, column 1), which the ordinarily skilled artisan would understand means that MART-1 was detected using by forming an avidin-biotin complex (ABC) comprising a biotinylated secondary antibody that binds the anti-MART-1 antibody and detectably labeled avidin.

Blessing et al. does not expressly teach a kit comprising the monoclonal antibody that binds specifically to MART-1, which is immobilized on a solid support (claim 23), wherein said support is latex (claim 24), and an anti-immunoglobulin antibody (claim 25), which kit can be used to detect MART-1 by means of detecting a radioisotope, fluorescent group, or enzyme (claim 26).

US Patent No. 6,232,086 B1 ('086) teaches a diagnostic kit comprising an antibody immobilized on a solid support, namely latex, which binds specifically to a cancer-associated antigen and is therefore usable to detect the antigen in a test sample, the presence of which antigen is diagnostic of cancer; see entire document, particularly column 22, line 57, through column 24, line 7. '086 teaches the kit can comprise, for example, a fluorescently or radioactively labeled secondary antibody that binds to the antibody that specifically binds the cancer-associated antigen (column 22, line 57, through column 24, line 7). '086 further teaches the kit can comprise an

antibody that is attached to an enzyme substrate, which can be used in an enzyme-linked immunosorbent assay (ELISA) (column 22, line 57, through column 24, line 7).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to formulate a kit for use in diagnosing melanocytic lesions, particularly malignant melanoma, by a process that comprises measuring the level of expression of MART-1 using an antibody that binds specifically to MART-1, which kit comprises, depending upon the type of immunoassay to be used, the antibody that binds specifically to MART-1, which can be immobilized on latex and fluorescently or radioactively labeled or attached to an enzyme substrate, and a secondary anti-immunoglobulin, which can be fluorescently or radioactively labeled or attached to an enzyme substrate, because '086 teaches that such kits can be formulated for diagnostic use. One ordinarily skilled in the art at the time of the invention would have been motivated to do so to provide an accessible and convenient means for diagnosing melanocytic lesions, particularly malignant melanoma.

## ***Conclusion***

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

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